CLAIMS

WHAT IS CLAIMED IS:

1. A method for modulating neurogenesis in neural tissue of a patient exhibiting at least one symptom of a central nervous system disorder selected from the group consisting of neurodegenerative disorders, ischemic disorders, neurological traumas, and learning and memory disorders, comprising: administrating at least one agent that elevates intracellular cAMP levels in the tissue, wherein the agent modulates neurogenesis in the patient, thereby modulating neurogenesis in the neural tissue of the patient.

2. The method of claim 1 wherein the agent is selected from the group consisting of a cAMP analog, an inhibitor of cAMP-specific phosphodiesterase, an adenylate cyclase activator, and an activator of ADP-ribosylation of a stimulatory G protein.

3. The method of claim 2 wherein said cAMP analog is selected from the group consisting of 8-pCPT-2-O-Me-cAMP, 8-Br-cAMP, Rp-cAMPS, 8-Cl-cAMP, Dibutyryl cAMP, pCPT-cAMP, and N6-monobutyryladenosine 3',5'-cyclic monophosphate.

4. The method of claim 2 wherein said inhibitor of cAMP-specific phosphodiesterase is selected from the group consisting of theophylline, 2,6-dihydroxy-1,3-dimethylpurine; 1,3-dimethylxanthine), caffeine, quercetin dihydrate, 4-(3-butoxy-4-methoxybenzyl)imidazolidin-2-one, propentofylline, 3-methyl-1-(5-oxohexyl)-7-propylxanthine), 3-Isobutyl-1-methylxanthine, IBMX,; 3-isobutyl-1-methyl-2,6(1H,3H)-purinedione, 1-methyl-3-isobutylxanthine, 8-Methoxymethyl-3-isobutyl-1-methylxanthine, enoximone, papaverine hydrochloride, calmidazolium chloride, imidazolium chloride, 1-[bis(4-chlorophenyl)methyl]-3-[2-(2,4-dichlorophenyl)-2-(2,4-dichlorobenzyloxy)ethyl]-1H-imidazolium chloride, SKF 94836, neuropeptide Y fragment 22-36, aminophylline hydrate, butein, papaverine hydrochloride, etazolate hydrochloride, trifluoperazine dihydrochloride, and milrinone.

5. The method of claim 2 wherein said adenylate cyclase activator is forskolin.

6. The method of claim 2 wherein said activator of ADP-ribosylation of a stimulatory G protein is selected from the group consisting of pertussis toxin and cholera toxin.

7. The method of claim 1 wherein said agent is selected from the group consisting of Adrenocortico-tropic hormone, Endothelin-1, MECA, HE-NECA, [Cys3,6, Tyr8, Pro9]-Substance P, [D-Arg0, Hyp3, Igl5, D-Igl7, Oic8]-Bradykinin, Adrenomedullin, [Des-Arg9, Leu8]-Bradykinin, [Des-Arg9]-Bradykinin, [D-Pen2-5]-Enkephalin, [D-pGlu1, D-Phe2, D-Trp3,6]-LH-RH, Adrenomedullin (26-52), Adrenomedullin (22-52), a -Neo-Endorphin, b-MSH, a-MSH, Thyrocalcitonin, Calcitonin, CART (61-102), Cholecystokinin Octapeptide [CCK(26-33)], DTLET, DDAVP, Eledoisin, g-MSH, a-Neurokinin, PACAP-38, Beta-ANP, Galanin (1-13)-Spantide-Amide, M40, [Sar9, Met (0)11]-Substance P, Sarafotoxin S6a, Sarafotoxin S6b, Sarafotoxin S6c, [Nle8,18, Tyr34]-Parathyroid Hormone (1-34) Amide, ACTH, Glucagon-Like Peptide-1 (7-37), Exendin-3, Exendin-4, Urotensin II, Vasoactive Intestinal Peptide, Nor-Binaltorphimine, and Agouti Related Protein (87-132)-Amide.

8. The method of claim 1 wherein said agent is selected from the group consisting of fenoldopam methanesulphonate, dopamine hydrochloride, apomorphine hydrochloride, histamine phosphate, ACTH, sumatriptan succinate, prostaglandin F2alpha tromethamine, prostaglandin E1, prostaglandin I2, iloprost tromethamine, prostaglandin E2, misoprostol, sulproston, ATP disodium salt, pindolol, secretin, cisapride, phentolamine methanesulphonate, nemonapride, clozapine, sertindole, olanzapine, risperidone, sulpiride, levosulpride,Chlorpromazine, chlorpromazine, hydrochloride, haloperidol, domperidone, fluphenazine dihydrochloride/decanoate/enantate, fluphenazine,, dihydrochloride/decanoate, fluphenazine dihydrochloride, ATP (adenosin triphosphate), ATP (adenosin triphosphate) disodium salt, ketanserin,ketanserin tartare, metergoline, pindolol, prazosin hydrochloride, Yohimbine, yohimbine hydrochloride, theophylline, caffeine, theobromine, aminophylline , amrinone, milrinone, naltrexone, naloxone, albuterol, levalbuterol, metaproterenol, terbutaline, pirbuterol, salmeterol, bitolterol, colterol, dobutamine, 8L-arginine-vasopressin, 8-lysine-vasopressin, desmopressin, methyldopa, DOPA, rauwolshine, prazosin, phentolamine, quinidine, dapiprazole, loxiglumide, chorionic gonadotropin, follitropin-alpha, follitropin–beta(FSH), menotropin (LH, FSH), oxytocin, somatostatin antagonists, RMP-7, ACE inhibitors

(like captopril), misoprostol, latanoprost, PGE1, alprostadil, somatropin (GH, PRL) secretagogues (MK-677), tabimorelin (NN-703, pamorelin, NNC-26-0323, TRH, cosyntropin, corticorelin, glucagon, enteroglucagon, PTH 1-34, cocaine, amphetamine, dextroamphetamine, metamphetamien, phenmetrazine, methylphenidate, diethylpropion, metyrosine, reserpine, minoxidil, sulfasalazine, levamisole, and thalidomide and fluoride.

9. The method of claim 1 wherein the nervous system disorder is selected from the group consisting of Parkinson's disease and Parkinsonian disorders, Huntington's disease, Alzheimer's disease, multiple sclerosis, amyotrophic lateral sclerosis, Shy-Drager syndrome, progressive supranuclear palsy, Lewy body disease, spinal ischemia, ischemic stroke, cerebral infarction, spinal cord injury, and cancer-related brain and spinal cord injury, multi-infarct dementia, and geriatric dementia.

10. The method of claim 1 wherein modulating neurogenesis is modulating proliferation, differentiation, migration or survival of a neural stem cells or progenitor cells in said neural tissue.

11. The method of claim 1 wherein said agent elevates the intracellular cAMP levels of said tissue above 20% as compared to a tissue not administered said agent.

12. The method of claim 1 wherein the agent is administered to the central nervous system of the patient.

13. The method of claim 1 wherein the agent is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

14. The method of claim 1 wherein the agent is administered by a liposome delivery system.

15. The method of claim 1 wherein said neurogenesis comprise maintaining or increasing the amount or percentage of doublecortin positive cells in the neural tissue relative to a patient not administered said agent.

16. The method of claim 1 wherein said modulating neurogenesis is performed by an activation of a GPCR receptor in said neural tissue.

17. A method for modulating neurogenesis in neural tissue of a patient exhibiting at least one symptom of a central nervous system disorder selected from the group consisting of neurodegenerative disorders, ischemic disorders, neurological traumas, and learning and memory disorders, comprising: administrating at least one agent that elevates intracellular Ca^{2+} levels in the tissue, wherein the agent induces neurogenesis in the patient, thereby modulating neurogenesis of cells in the neural tissue of the patient.

18. The method of claim 17 wherein the agent is selected from the group consisting of Amylin Receptor Antagonist/Calcitonin(8-32), ANP, CGRP (8-37), Endothelin-1, g-MSH, Growth Hormone Releasing Factor, MGOP 27, PACAP-38 , Sarafotoxin S6a, Sarafotoxin S6b, Sarafotoxin S6c, Septide, Somatostatin-28, Cholera toxin from Vibrio Cholerae, Angiotensin II, [D-Pen2-5]-Enkephalin, Adrenomedullin, Endothelin-1.

19. The method of claim 17 wherein the nervous system disorder is selected from the group consisting of Parkinson's disease and Parkinsonian disorders, Huntington's disease, Alzheimer's disease, multiple sclerosis, amyotrophic lateral sclerosis, Shy-Drager syndrome, progressive supranuclear palsy, Lewy body disease, spinal ischemia, ischemic stroke, cerebral infarction, spinal cord injury, and cancer-related brain and spinal cord injury, multi-infarct dementia, and geriatric dementia.

20. The method of claim 17 wherein modulating neurogenesis is modulating proliferation, differentiation, migration or survival of a neural stem cells or progenitor cells in said neural tissue.

21. The method of claim 17 wherein the agent is administered to the central nervous system of the patient.

22. The method of claim 17 wherein the agent is administered to achieve a tissue concentration of 0.0001 nM to 50 nM.

23. The method of claim 17 wherein the agent is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

24. The method of claim 17 wherein the agent is administered by a liposome delivery system.

25. The method of claim 17 wherein said neurogenesis comprise increasing or maintaining the amount or percentage of doublecortin positive cells in the neural tissue of the patient relative to a patient not administered the agent.

26. A method for increasing the intracellular levels of cAMP in a cell, comprising contacting said cell with an effective amount of an agent selected from the group consisting of (Des-Arg9,Leu8)-Bradykinin, (Des-Arg9)-Bradykinin, Alpha-NeoEndorphin, CART (61-102), DTLET, Eledoisin, Urotensin II, [Nle8,18, Tyr34]-Parathyroid Hormone (1-34) Amide, [Cys3,6, Tyr8, Pro9]-Substance P and a combination thereof, whereby the intracellular level of cAMP in said cell is increased.

27. A method for stimulating intracelluar cAMP in a cell of a patient, comprising administering to said patient an effective amount of an agent from the group consisting of (Des-Arg9,Leu8)-Bradykinin, (Des-Arg9)-Bradykinin, Alpha-NeoEndorphin, CART (61-102), DTLET, Eledoisin, Urotensin II, [Nle8,18, Tyr34]-Parathyroid Hormone (1-34) Amide, [Cys3,6, Tyr8, Pro9]-Substance P and a combination thereof, whereby the intracellular level of cAMP in said cell is increased.

28. The method of claim 27 wherein said cell is a cell from a neural tissue.

29. The method of claim 27 wherein said cell is a neural stem cell or a neural progenitor cell.

30. The method of claim 27 wherein said effective amount of agent modulates neurogenesis in said neural tissue.

31. The method of claim 27 which increases the amount or percentage of doublecortin positive cells in said neural tissue.

32. A method for modulating neurogenesis in vitro comprising the steps of:

a) culturing a population of neural cells comprising neural stem cells;

b) adding to the cultured cells at least one neurogenesis modulating agent;

c) repeating steps b until a desired level of neurogenesis in achieved.

33. The method of claim 32 wherein step (b) elevates intracellular cAMP level of said neural stem cells at least 20%.

34. The method of claim 32 wherein the stem cell is isolated from tissue selected from the group consisting of cortex, olfactory tubercle, retina, septum, lateral ganglionic eminence, medial ganglionic eminence, amygdala, hippocampus, thalamus, hypothalamus, ventral and dorsal mesencephalon, brain stem, cerebellum, spinal cord.

35. The method of claim 32 wherein the stem cell is isolated from a mammal.

36. The method of claim 32 wherein said neurogenesis comprises increasing or maintaining the amount or percentage of doublecortin positive cells in said population of neural cells.

37. The method of claim 35 wherein the mammal is a human.